201-14528

NCIC HPV
Sent by: Mary-Beth Weaver

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To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Environmental Defense comments on Propargyl Alcohol (CAS# 107-19-7)

Richard_Denison@environmentaldefense.org on 06/02/2003 02:01:46 PM

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Subject: Environmental Defense comments on Propargyl Alcohol (CAS# 107-19-7)

(Submitted via Internet 6/2/03 to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and erauckman@charter.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for Propargyl Alcohol (CAS# 107-19-7).

The test plan and robust summaries were prepared by the Toxicology and Regulatory Affairs Group of the Propargyl Alcohol (PA) Consortium. PA is a relatively toxic compound that is synthesized through several different pathways. It is used as a chemical intermediate, corrosion inhibitor, solvent stabilizer, soil fumigant and polymer modifier. The test plan states that PA is not used in consumer products although the uses indicated above would seem to contradict this statement.

The test plan and robust summaries are complete, accurate and do a very credible job in justifying conclusions made in the test plan. The test plan and robust summaries represent an excellent example for others to follow in the preparation of HPV submissions. We agree with all of the sponsor's conclusions, including the proposal to conduct a combined reproductive/ developmental toxicity study on PA. Specific comments are as follows:

1. PA is a toxic chemical, so potential workplace exposures are of concern. The ACGIH-TLV is 1 ppm. Has the sponsor collected data on workplace exposures? If so, they should be made available.

2. The test plan and robust summaries include an excellent description of the metabolism of PA and a plausible mechanism for PA-mediated liver and kidney toxicity. The mechanism seems to involve metabolism to a reactive aldehyde catalyzed by a specific form of cytochrome P-450. Although this level of information is not required by the HPV program, it is very helpful to companies and regulatory agencies in the development of scientifically-credible risk assessments.

3. Available data indicate that PA partitions into water and that it is rapidly biodegraded. The sponsor asserts that PA is completely degraded by wastewater treatment, but no data are provided on the range of levels detected or predicted in wastewater before and after treatment. If such data are available, they should be included in the test plan because PA exhibits significant toxicity to aquatic organisms.

4. Ecotoxicity data are sufficient to fulfill HPV requirements. PA, like its structural analog allyl alcohol, is toxic to fish.

5. Acute toxicity studies were not conducted according to GLP, but we agree

with the sponsor that additional studies would constitute an unnecessary use of animals since other available information is sufficient and the NTP studies provide data on the maximally-tolerated dose.

6. Several well-conducted repeat dose studies are available, including 14- and 90-day inhalation studies conducted by the NTP. These data involve multiple species and are more than adequate to fulfill requirements of the HPV program. They indicate a NOEL range of 4-32 ppm depending on the endpoint evaluated. The most sensitive endpoint was the respiratory epithelium.

7. Genetic toxicity data indicate that PA has weak or no genotoxic activity. In any event, existing data are sufficient to fulfill HPV requirements. The NTP is currently conducting a cancer bioassay on PA and the sponsor is clearly aware of this study and keeping up with results as they become available. These results will permit the genetic toxicity data to be placed in proper context.

8. The sponsor indicates that no reproductive or developmental toxicity studies are available on PA, and hence they propose to conduct a combined reproductive/developmental toxicity study. We agree with this proposal; we also note that histology slides from the NTP studies are available in the NTP archives and may provide a useful resource in interpreting results from the proposed study when it is completed.

Thank you for this opportunity to comment.

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